

WHAT IS CLAIMED IS:

- 1 1. A method for producing a non-human animal model of a human or non-human  
2 animal disease which comprises transferring at least one aberrant form of at least one  
3 gene known to be associated with said disease in humans or non-human animals into  
4 appropriate tissue of a living non-human animal under conditions which result in the  
5 expression of said at least one aberrant gene, wherein said transferring does not require  
6 the modification of the germ-line of said living animal.  
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- 1 2. The method according to claim 1 wherein said human or non-human animal  
2 disease is a neurodegenerative disease.  
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- 1 3. The method according to claim 2 wherein said human disease is selected from the  
2 group consisting of Alzheimer's Disease, Parkinson's Disease, and Huntington's Disease.  
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- 1 4. The method according to claim 3 wherein said at least one gene is an aberrant  
2 form of tau.  
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- 1 5. The method according to claim 3 wherein said aberrant form of tau is P301L,  
2 associated with "fronto-temporal dementia with Parkinson's linked to chromosome 17  
3 (FTDP-17)".  
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- 1 6. The method according to claim 3 wherein said at least one gene is an aberrant  
2 form of alpha-synuclein.  
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- 1 7. The method according to claim 6 wherein said aberrant form of alpha-synuclein is  
2 mutant  $\alpha$ -synuclein (A30P), associated with Parkinson's Disease.  
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- 1 8. The method according to claim 3 wherein said at least one gene is a mutant  
2 amyloid precursor protein (APP), a mutant presenilin-1 (PS1), or combinations thereof,  
3 associated with Alzheimer's Disease.  
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1 9. The method according to claim 1 which comprises identifying a combination of  
2 genes relevant to a particular human pathology and somatically transferring combinations  
3 of said genes into tissues appropriate to said particular human pathology in a non-human  
4 animal model appropriate to said human pathology.

1 10. The method according to claim 1 comprising:

- 2 (a) controlling the location to which the genes are transferred, that is spatially  
3 controlling gene expression of the transferred genes, in the non-human animal  
4 model to which said at least one gene is transferred;
- 5 (b) controlling the temporal effects of transferred genes at specific times in the  
6 development of otherwise normal organisms, or in the development of organisms  
7 in which germline modifications have previously been made, by selecting the time  
8 at which said transferred genes are introduced into said organism, or by  
9 controlling the time of expression of said transferred genes;
- 10 (c) evaluating the effects of expression of combinations of multiple transgenes, which  
11 in a germline transgenic non-human animal would be difficult if not impossible to  
12 achieve due to diseases which might prevent the animal model from maturing to  
13 the age-appropriate state for modeling onset of a particular, complex human  
14 disease;
- 15 (d) increasing the rate for analyzing multiple genes which contribute to complex,  
16 multifactorial human diseases by transferring more than a single gene into an  
17 appropriate non-human animal model for said disease;
- 18 (e) testing pharmaceutical agents for their ability to ameliorate specific diseases  
19 induced in said non-human animal model;
- 20 (f) studying specific human pathologies induced in said non-human animal model by  
21 inducing said pathology in said animal model by transferring said at least one  
22 gene into said animal model;
- 23 (g) supplementing an existing germline transgenic model with additional somatically  
24 provided gene products to modulate the transgenic model;
- 25 (h) creating a disease condition in an otherwise healthy animal; and  
26 (i) combinations of (a) –(h).

1 11. A non-human animal produced by the method of claim 1.

1 12. A pharmaceutical identified through testing of pharmaceutical compounds  
2 using the non-human animal produced according to claim 11.

1 13. A method for inducing neurofibrillary tangles in the brain of a non-human  
2 animal which comprises injecting into the brain of said animal an effective amount of  
3 a gene expression construct encoding tau, alpha-synuclein, presenilin-1, amyloid  
4 precursor protein, IL6, or a combination thereof.

1 14. A non-human animal produced according to the method of claim 13.

1 15. A method for inducing behavioral changes in a non-human animal model  
2 which comprises somatic administration of at least one gene directly to the brain of  
3 said non-human animal, wherein said at least one gene is associated with a human  
4 neurodegenerative disease.

1 16. The method according to claim 1 wherein said at least one aberrant form  
2 of said at least one gene is transferred by means of an adeno-associated virus.

1 17. A composition comprising at least one gene construct adapted for  
2 producing a non-human animal model of a human or non-human-animal disease by  
3 transferring at least one aberrant form of at least one gene known to be associated  
4 with said disease in humans or non-human animals into appropriate tissue of a living  
5 non-human animal under conditions which result in the expression of said at least one  
6 aberrant gene, wherein said transferring does not require the modification of the  
7 germ-line of said living animal, said composition comprising said at least one  
8 aberrant gene in a vector construct which results in active expression of said gene  
9 upon introduction into said tissue.

1 18. The composition according to claim 17 wherein said at least one gene is  
2 an aberrant form of tau.

1 19. The composition according to claim 18 wherein said aberrant form of tau  
2 is P301L, associated with “fronto-temporal dementia with Parkinson’s linked to  
3 chromosome 17 (FTDP-17)”.

1 20. The composition according to claim 17 wherein said at least one gene is  
2 an aberrant form of alpha-synuclein.

1 21. . The composition according to claim 20 wherein said aberrant form of  
2 alpha-synuclein is mutant  $\alpha$ -synuclein (A30P), associated with Parkinson’s Disease.

1 22. . The composition according to claim 17 wherein said at least one gene is a  
2 mutant amyloid precursor protein (APP), a mutant presenilin-1 (PS1), or  
3 combinations thereof, associated with Alzheimer’s Disease.

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